CLAIMS

1. A method of diagnosing or prognosticating a neurodegenerative disease in a subject, or determining whether a subject is at increased risk of developing said disease, comprising:
determining a level and/or an activity of
(i) a transcription product of a gene coding for HIF3a, and/or
(ii) a translation product of a gene coding for HIF3a, and/or
(iii) a fragment, or derivative, or variant of said transcription and/or translation product, in a sample obtained from said subject and
comparing said level or said activity, or both said level and said activity of said transcription product and/or said translation product to a reference value representing a known disease status and/or to a reference value representing a known health status, and said level and/or said activity is varied or altered compared to a reference value representing a known health status, and/or is similar or equal to a reference value representing a known disease status, thereby diagnosing or prognosticating said neurodegenerative disease in said subject, or determining whether said subject is at increased risk of developing said neurodegenerative disease.

2. The method according to claim 1 wherein said neurodegenerative disease is Alzheimer's disease.

3. A kit for diagnosing or prognosticating a neurodegenerative disease, in particular Alzheimer's disease, in a subject, or determining the propensity or predisposition, the risk of a subject to develop such a disease, said kit comprising:
(a) at least one reagent which is selected from the group consisting of (i) reagents that selectively detect a transcription product of a gene coding for HIF3a and (ii) reagents that selectively detect a translation product of a gene coding for HIF3a;
whereby the diagnosis or prognosis or determination of the risk to develop Alzheimer's disease is determined by the steps of (i) detecting in a sample obtained from said subject a level, or an activity, or both said level and said activity of a transcription product and/or of a translation product of a gene coding for HIF3a, and (ii) comparing said level or activity, or both said level and said activity of a transcription product and/or of a translation product of a gene coding for HIF3a to a reference value representing a known health status and/or to a reference value representing a known disease status, and said level, or activity, or

both said level and said activity, of said transcription product and/or said translation product is varied compared to a reference value representing a known health status, and/or is similar or equal to a reference value representing a known disease status.

4. A genetically altered non-human animal comprising a non-native gene sequence coding for HIF3a, or a fragment, or a derivative, or a variant thereof.

5. The genetically altered non-human animal according to claim 4 wherein said non-human animal is a mammal, preferably a rodent, more preferably a mouse, a rat or a guinea pig, or an invertebrate animal, preferably an insect, more preferably a fly such as the fly *Drosophila melanogaster.*

6. The genetically altered non-human animal according to claims 4 and 5, wherein the expression of said genetic alteration results in said non-human animal exhibiting a predisposition to developing symptoms, and/or displaying symptoms of neuropathology similar to a neurodegenerative disease, in particular symptoms similar to AD.

7. The genetically altered non-human animal according to claims 4 and 5, wherein the expression of said genetic alteration results in said non-human animal which has a reduced risk of developing symptoms similar to a neurodegenerative disease, in particular a reduced risk of developing symptoms similar to AD and/or which shows a reduction of AD symptoms and/or which has no AD symptoms due to an effect caused by the expression of the gene used to genetically alter said non-human animal.

8. Use of the genetically altered non-human animal according to claims 4 to 7 for screening, testing, and validating compounds, agents, and modulators in the development of diagnostics and therapeutics to treat neurodegenerative diseases, in particular Alzheimer's disease.

9. A modulator of an activity and/or of a level of at least one substance which is selected from the group consisting of

(i) a gene coding for HIF3a, and/or
(ii) a transcription product of a gene coding for HIF3a, and/or
(iii) a translation product of a gene coding for HIF3a, and/or

(iv) a fragment, or derivative, or variant of (i) to (iii).

10. An assay for screening for a modulator of neurodegenerative diseases, in particular Alzheimer's disease, or related diseases or disorders of one or more substances selected from the group consisting of

(i) a gene coding for HIF3a, and/or

(ii) a transcription product of a gene coding for HIF3a, and/or

(iii) a translation product of a gene coding for HIF3a, and/or

(iv) a fragment, or derivative, or variant of (i) to (iii),

said method comprising:

(a) contacting a cell with a test compound;

(b) measuring the activity and/or level of one or more substances recited in (i) to (iv);

(c) measuring the activity and/or level of one or more substances recited in (i) to (iv) in a control cell not contacted with said test compound; and

(d) comparing the levels and/or activities of the substance in the cells of step (b) and (c), wherein an alteration in the activity and/or level of substances in the contacted cells indicates that the test compound is a modulator of said diseases or disorders.

11. A method of screening for a modulator of neurodegenerative diseases, in particular Alzheimer's disease, or related diseases or disorders of one or more substances selected from the group consisting of

(i) a gene coding for HIF3a, and/or

(ii) a transcription product of a gene coding for HIF3a, and/or

(iii) a translation product of a gene coding for HIF3a, and/or

(v) a fragment, or derivative, or variant of (i) to (iii),

said method comprising:

(a) administering a test compound to a test animal which is predisposed to developing or has already developed symptoms of a neurodegenerative disease or related diseases or disorders in respect of the substances recited in (i) to (iv);

(b) measuring the activity and/or level of one or more substances recited in (i) to (iv);

(c) measuring the activity and/or level of one or more substances recited in (i) or (iv) in a matched control animal which is predisposed to developing or has already developed symptoms of a neurodegenerative disease or related

diseases or disorders in respect to the substances recited in (i) to (iv) and to which animal no such test compound has been administered;

(d) comparing the activity and/or level of the substance in the animals of step (b) and (c), wherein an alteration in the activity and/or level of substances in the test animal indicates that the test compound is a modulator of said diseases or disorders.

12. The method according to claim 11 wherein said test animal and/or said control animal is a genetically altered non-human animal which expresses the gene coding for HIF3a, or a fragment, or a derivative, or a variant thereof, under the control of a transcriptional control element which is not the native HIF3a gene transcriptional control element.

13. An assay for testing a compound, preferably for screening a plurality of compounds to determine the degree of binding of said compounds to a HIF3a translation product, or to a fragment, or derivative, or variant thereof, said assay comprising the steps of:

(i) adding a liquid suspension of said HIF3a translation product, or a fragment, or derivative, or variant thereof, to a plurality of containers;

(ii) adding a detectable, in particular a fluorescently labelled compound or a plurality of fluorescently labelled compounds to be screened for said binding to said plurality of containers;

(iii) incubating said HIF3a translation product, or said fragment, or derivative, or variant thereof, and said detectable, in particular fluorescently labelled compound or fluorescently labelled compounds;

(iv) measuring amounts of preferably fluorescence associated with said HIF3a translation product, or with said fragment, or derivative, or variant thereof; and

(v) determining the degree of binding by one or more of said compounds to said HIF3a translation product, or said fragment, or derivative, or variant thereof.

14. Use of protein molecules of SEQ ID NO. 2, SEQ ID NO. 3, SEQ ID NO. 4, SEQ ID NO. 5, said protein molecules being translation products of the gene coding for HIF3a, or fragments, or derivatives, or variants thereof, as diagnostic targets for detecting a neurodegenerative disease, preferably Alzheimer's disease.

15. Use of protein molecules of SEQ ID NO. 2, SEQ ID NO. 3, SEQ ID NO. 4, SEQ ID NO. 5, said protein molecules being translation products of the gene coding for HIF3a, or fragments, or derivatives, or variants thereof, as screening targets for reagents or compounds preventing, or treating, or ameliorating a neurodegenerative disease, preferably Alzheimer's disease.

16. Use of an antibody specifically immunoreactive with an immunogen, wherein said immunogen is a translation product of a gene coding for HIF3a, SEQ ID NO. 2, SEQ ID NO. 3, SEQ ID NO. 4, SEQ ID NO. 5, or a fragment, or derivative, or variant thereof, for detecting the pathological state of a cell in a sample obtained from a subject, comprising immunocytochemical staining of said cell with said antibody, wherein an altered degree of staining, or an altered staining pattern in said cell compared to a cell representing a known health status indicates a pathological state of said cell which relates to a neurodegenerative disease, preferably to Alzheimer's disease.